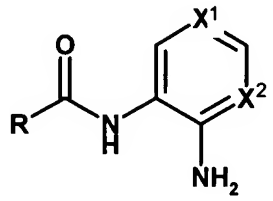
Claims

1. A pharmaceutical composition comprising, as an active ingredient, one or more compounds represented by the formula



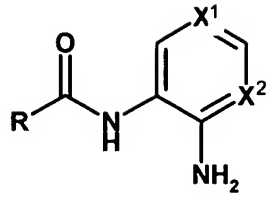
(I)

or a pharmaceutically acceptable salt or prodrug thereof,
wherein
$X^1$ and $X^2$ are each independently selected from a CH group or a nitrogen atom; and
R is an optionally substituted five or six membered nonaromatic carbocyclic ring or an nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring; provided that R is not an optionally substituted pyridinyl.

2. The composition of claim 1 further comprising a pharmaceutically acceptable excipient or diluent.

3. The composition of claim 1 wherein the compound is selected from the group consisting of
Benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-phenyl)-amide;
5-Propoxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
5-Allyloxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
7-Methoxy-benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
7-Methoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-phenyl)-amide; and
Thiazole-4-carboxylic acid (2-amino-phenyl)-amide.

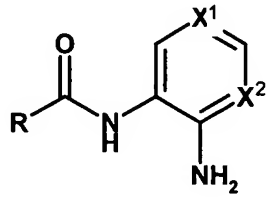
4. A compound of the formula



(I)

or a pharmaceutically acceptable salt or prodrug thereof,
wherein
$X^1$ and $X^2$ are CH groups; and
R is an optionally substituted five or six membered nonaromatic carbocyclic ring or an nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring; and
provided that R is not a halogenated benzothiophene; halogenated thiazolyl; N-benzyl-2-acetylamino-4,5-dimethylpyrrole-3-yl; optionally substituted 1,4-oxathiine-3-yl; optionally substituted pyridinyl; pyridazine-5-yl which is substituted by one to three substituents selected from methyl, methoxy, methoxycarbonyl or carboxyl.

5. A compound of the formula



(I)

or a pharmaceutically acceptable salt or prodrug thereof,
wherein
one of $X^1$ or $X^2$ is a nitrogen atom, and the other is a CH group; and
R is an optionally substituted five or six membered nonaromatic carboxcyclic ring or a nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring; and
provided that R is not an optionally substituted pyridinyl.

6. The compound of claim 5 wherein $X^1$ and $X^2$ are both nitrogen atoms.

7. The compound of claim 5, wherein the compound is selected from the group consisting of

5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-phenyl)-amide;
5-Propoxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
5-Allyloxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
7-Methoxy-benzofuran-2-carboxylic acid (2-amino-phenyl)-amide; and
7-Methoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-phenyl)-amide.

8. A compound selected from the group consisting of

Furan-2-carboxylic acid (2-amino-phenyl)-amide;
1-Methyl-1H-pyrrole-2-carboxylic acid (2-amino-phenyl)-amide;
3,5-Dimethyl-isoxazole-4-carboxylic acid (2-amino-phenyl)-amide;
5-Oxo-pyrrolidine-2-carboxylic acid (2-amino-phenyl)-amide;
1H-Pyrrole-2-carboxylic acid (2-amino-phenyl)-amide;
5-Methyl-3-phenyl-isoxazole-4-carboxylic acid (2-amino-phenyl)-amide;
5-Phenethyl-4,5-dihydro-isoxazole-3-carboxylic acid (2-amino-phenyl)-amide;
5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-phenyl)-amide; and
3-Methyl-isoxazole-5-carboxylic acid (2-amino-phenyl)-amide.

9. A compound selected from the group consisting of

2,5-Dimethyl-2h-pyrazole-3-carboxylic acid (2-amino-phenyl)-amide;
1,5-Dimethyl-1H-pyrazole-3-carboxylic acid (2-amino-phenyl)-amide;
5-Propoxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
5-Allyloxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
3H-Benzo[e]indole-2-carboxylic acid (2-aminophenyl)-amide;
5-Methyl-2H-pyrazole-3-carboxylic acid (2-amino-phenyl)-amide;
3-Phenyl-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
3-Methyl-5-phenyl-isoxazole-4-carboxylic acid (2-amino-phenyl)-amide;
1-Acetyl-piperidine-4-carboxylic acid (2-amino-phenyl)-amide; and
Cyclohex-1-enecarboxylic acid (2-amino-phenyl)-amide.

10. A compound selected from the group consisting of
3-(2-Methoxy-ethoxy)-thiophene-2-carboxylic acid (2-amino-phenyl)-amide;
1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxylic acid (2-amino-phenyl)-amide;
7-Methoxy-benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
1H-Imidazole-2-carboxylic acid (2-1mino-phenyl)-amide;
5-(4-Chloro-phenyl)-1H-pyrazole-3-carboxylic acid (2-amino-phenyl)-amide;
7-Methoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-phenyl)-amide;
2-Phenyl-2H-[1,2,3]triazole-4-carboxylic acid (2-amino-phenyl)-amide;
2-Chloro-thiazole-4-carboxylic acid (2-amino-phenyl)-amide;
2-Benzyl-5-methyl-2H-pyrazole-3-carboxylic acid (2-amino-phenyl)-amide; and
5-Methyl-1-phenyl-1H-pyrazole-3-carboxylic acid (2-amino-phenyl)-amide.

11. A compound selected from the group consisting of
5-Methyl-1-phenyl-1H-[1,2,3]triazole-4-carboxylic acid (2-amino-phenyl)-amide;
5-Methyl-2-phenyl-oxazole-4-carboxylic acid (2-amino-phenyl)-amide;
2,5-Dimethyl-4-nitro-2H-pyrazole-3-carboxylic acid (2-amino-phenyl)-amide;
1H-Indole-2-carboxylic acid (2-amino-phenyl)-amide;
4-Acetyl-3,5-dimethyl-1H-pyrrole-2-carboxylic acid (2-amino-phenyl)-amide;
6-Oxo-1,4,5,6-tetrahydro-pyridazine-3-carboxylic acid (2-amino-phenyl)-amide;
5-Phenyl-isoxazole-3-carboxylic acid (2-amino-phenyl)-amide;
Benzofuran-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide; and
Furan-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide.

12. A compound selected from the group consisting of
3,5-Dimethyl-isoxazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
5-Oxo-pyrrolidine-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
5-Methyl-3-phenyl-isoxazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
2,5-Dimethyl-2H-pyrazole-3-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
1,5-Dimethyl-1H-pyrazole-3-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
5-Propoxy-1H-indole-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
5-Allyloxy-1H-indole-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;

3H-Benzo[e]indole-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide; and
5-Methyl-2H-pyrazole-3-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide.

13. A compound selected from the group consisting of
1-Acetyl-piperidine-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
Cyclohex-1-enecarboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
3-(2-Methoxy-ethoxy)-thiophene-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
7-Methoxy-benzofuran-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
7-Methoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
2-Phenyl-2H-[1,2,3]triazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
5-Phenyl-thiazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
2-Chloro-thiazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide; and
2-Benzyl-5-methyl-2H-pyrazole-3-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide.

14. A compound selected from the group consisting of
5-Methyl-1-phenyl-1H-pyrazole-3-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
5-Methyl-1-phenyl-1H-[1,2,3]triazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
5-Methyl-2-phenyl-oxazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
1H-Indole-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
4-Acetyl-3,5-dimethyl-1H-pyrrole-2-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;;
6-Oxo-1,4,5,6-tetrahydro-pyridazine-3-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
Thiazole-4-carboxylic acid (2-amino-4,5-dichloro-phenyl)-amide;
Benzofuran-2-carboxylic acid (2-amino-pyridin-3-yl)-amide;
5-Phenethyl-4,5-dihydro-isoxazole-3-carboxylic acid (2-amino-pyridin-3-yl)-amide; and
5-Allyloxy-1H-indole-2-carboxylic acid (2-amino-pyridin-3-yl)-amide.

15. A compound selected from the group consisting of
Cyclohex-1-enecarboxylic acid (2-amino-pyridin-3-yl)-amide;
1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxylic acid (2-amino-pyridin-3-yl)-amide;

7-Methoxy-benzofuran-2-carboxylic acid (2-amino-pyridin-3-yl)-amide;
7-Methoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-pyridin-3-yl)-amide;
2-Phenyl-2H-[1,2,3]triazole-4-carboxylic acid (2-amino-pyridin-3-yl)-amide;
5-Phenyl-thiazole-4-carboxylic acid (2-amino-pyridin-3-yl)-amide;
2-Benzyl-5-methyl-2H-pyrazole-3-carboxylic acid (2-amino-pyridin-3-yl)-amide;
5-Methyl-1-phenyl-1H-[1,2,3]triazole-4-carboxylic acid (2-amino-pyridin-3-yl)-amide;
5-Methyl-2-phenyl-oxazole-4-carboxylic acid (2-amino-pyridin-3-yl)-amide; and
2,5-Dimethyl-4-nitro-2H-pyrazole-3-carboxylic acid (2-amino-pyridin-3-yl)-amide.

16. A compound selected from the group consisting of
Benzofuran-2-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
5-Phenethyl-4,5-dihydro-isoxazole-3-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
Cyclohex-1-enecarboxylic acid (4-amino-pyrimidin-5-yl)-amide;
3-(2-Methoxy-ethoxy)-thiophene-2-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
7-Methoxy-benzofuran-2-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
7-Methoxy-benzo[b]thiophene-2-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
2-Phenyl-2H-[1,2,3]triazole-4-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
5-Phenyl-thiazole-4-carboxylic acid (4-amino-pyrimidin-5-yl)-amide; and
2-Benzyl-5-methyl-2H-pyrazole-3-carboxylic acid (4-amino-pyrimidin-5-yl)-amide.

17. A compound selected from the group consisting of
5-Methyl-1-phenyl-1H-[1,2,3]triazole-4-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
5-Methyl-2-phenyl-oxazole-4-carboxylic acid (4-amino-pyrimidin-5-yl)-amide;
5-methoxy-benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
6,7-dimethyl-benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
5-nitro-benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
6-methoxy-benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
6-methoxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
4-chloro-5-methoxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
3-methoxy-5-methyl-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide; and
3-pyrrol-1-yl-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide.

18. A compound selected from the group consisting of

7-nitro-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;

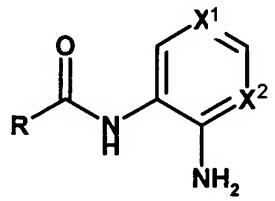
5,7-dimethoxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;

5-Methoxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;

6-Methoxy-4-trifluoromethyl-1*H*-indole-2-carboxylic acid (2-amino-phenyl)-amide; and

5-Methoxy-1-methyl-3-methylsulfanyl-1*H*-indole-2-carboxylic acid (2-amino-phenyl)-amide.

19. A process for manufacturing a compound of the formula




(I)

or a pharmaceutically acceptable salt or prodrug thereof,

wherein

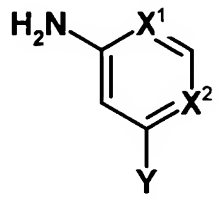
$X^1$ and $X^2$ are CH groups; and

R is an optionally substituted five or six membered nonaromatic carbocyclic ring or an nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring; provided that R is not a halogenated benzothiophene; halogenated thiazolyl; N-benzyl-2-acetylamino-4,5-dimethylpyrrole-3-yl; optionally substituted1,4-oxathiine-3-yl; optionally substituted pyridinyl; or pyridazine-5-yl which is substituted by one to three substituents selected from methyl, methoxy, methoxycarbonyl or carboxyl;

by reacting a carboxylic acid of the formula


II

wherein R is an optionally substituted five or six membered nonaromatic carbocyclic ring or an nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring;
with a compound of the formula



III

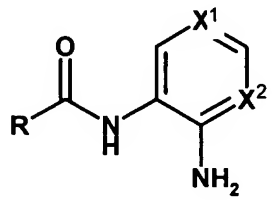
wherein
Y is a nitro-, amino- or a protected amino group; in the presence of activation reagents.

20. The process of claim 19 wherein the six membered ring is substituted by at least one halogen.

21. The process of claim 19 further comprising the formation of an amino group by either cleaving a protection group or reduction of a nitro group.

22. The process of claim 19 further comprising converting the compound to a pharmaceutically acceptable salt.

23. A process of manufacturing a compound of the formula



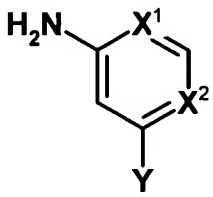
(I)

or a pharmaceutically acceptable salt or prodrug thereof,
wherein

one of $X^1$ or $X^2$ is a nitrogen atom and the other is a CH group; and
R is an optionally substituted five or six membered nonaromatic carbocyclic ring or an nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring; provided that R is not an optionally substituted pyridinyl;
by reacting a carboxylic acid of the formula

II

wherein R is an optionally substituted five or six membered nonaromatic carbocyclic ring or an nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring;
with a compound of the formula



III

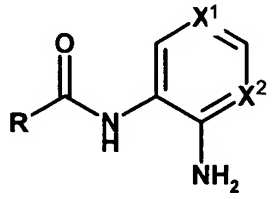
wherein Y is a nitro-, amino- or a protected amino group; in the presence of an activation reagent.

24. The process of claim 23 wherein both $X^1$ and $X^2$ are nitrogen atoms.

25. The process of claim 23 further comprising the formation of an amino group by either cleaving a protection group or reduction of a nitro group.

26. The process of claim 23 further comprising converting the compound to a pharmaceutically acceptable salt.

27. A method for treating cancer comprising administering to a patient in need of such treatment an effective amount of at least one compound of



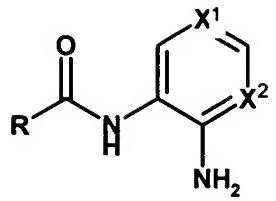

(I)

or a pharmaceutically acceptable salt or prodrug thereof,
wherein
$X^1$ and $X^2$ are each independently selected from a CH group or a nitrogen atom; and
R is an optionally substituted five or six membered nonaromatic carbocyclic ring or a nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring.

28. The method of claim 27 wherein the compound is a histone acetylation-inducing agent.

29. The method of claim 27 wherein the compound isselected from the group consisting of
Benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
5,6-Dimethoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-phenyl)-amide;
5-Propoxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
5-Allyloxy-1H-indole-2-carboxylic acid (2-amino-phenyl)-amide;
7-Methoxy-benzofuran-2-carboxylic acid (2-amino-phenyl)-amide;
7-Methoxy-benzo[b]thiophene-2-carboxylic acid (2-amino-phenyl)-amide; and
Thiazole-4-carboxylic acid (2-amino-phenyl)-amide.

30. A method for treating tumor cell profliferation comprising inducing histone acetylation in a tumor cell, due to administering to the tumor cell an effective amount of at least one compound of




(I)

or a pharmaceutically acceptable salt or prodrug thereof,

wherein

$X^1$ and $X^2$ are each independently selected from a CH group or a nitrogen atom; and

R is an optionally substituted five or six membered nonaromatic carbocyclic ring or a nonaromatic or aromatic heterocyclic ring, whereby the ring is optionally condensed with a 6-membered, optionally substituted carbocyclic aromatic ring.